

Chapter 17

An Investment Case for Ending Neglected Tropical Diseases

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Box 17.1

Key Messages

- Neglected tropical diseases (NTDs) together account for a significant and inequitably distributed global disease burden, similar in order of magnitude to those of tuberculosis or malaria at approximately 22 million disability-adjusted life-years (DALYs) in 2012.
- Cost-effective interventions to end NTDs are available for as little as US\$3 per DALY averted; these interventions reach the poorest and most marginalized populations and provide an integrated approach to treat multiple diseases.
- Ambitious eradication, elimination, and control targets for individual diseases emerged with the launch of the World Health Organization's NTD roadmap in 2012; the Sustainable Development Goals target "the end of NTDs" by 2030.
- Interventions to end NTDs are affordable globally; estimated treatment costs are US\$750 million per year for 2015 to 2020 and US\$300 million per year for 2020 to 2030.
- Interventions to end NTDs are affordable for the governments of most endemic countries; treatment and vector control combined require less than 0.1 percent of domestic health spending. Domestic value for money is enhanced by the unprecedented scale of the London Declaration donation of medicines for nine of the most prevalent NTDs.
- Reaching those targets could avert an estimated 519 million DALYs from 2015 to 2030, compared to 1990 and the beginning of concerted efforts to control NTDs.
- The benefit to affected individuals in terms of averted out-of-pocket health expenditures and lost productivity exceeds US\$342 billion over the same period.
- The net benefit to affected individuals is about US\$25 for every dollar to be invested by public and philanthropic funders between 1990 and 2030—a 30 percent annualized rate of return.
- The end of NTDs represents a fair and efficient transfer toward universal health coverage and social protection for those who are least well-off.

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INTRODUCTION

The neglected tropical diseases (NTDs) affect more than 1 billion of the poorest and most marginalized people of the world. These infections are a consequence of the environmental and socioeconomic conditions in which the poor live, and the ill health and disability they cause are a primary factor locking the poor into poverty. They are diseases of the most neglected people who live in countries that lack the basic resources to control them. Yet this chapter demonstrates that the tools to end this neglect already exist, and that there are compelling economic arguments that ending these diseases would be one of the most cost-effective of global public health programs.

The NTD concept was developed to draw attention to this opportunity that was overlooked by the Millennium Development Goals (MDGs). At least 18 diseases are recognized as NTDs by World Health Assembly resolutions; the latest addition is mycetoma (WHO 2013, 2016). The World Health Organization (WHO) has set specific targets for control, elimination, and eradication of a subset of these diseases (table 17.1). These are the NTDs that we focus on in this chapter. The end of NTDs

is now firmly embedded within the Sustainable Development Goals (SDGs) for 2030, under target 3.3, reflecting the promise to “leave no one behind.”

This chapter reaffirms the case that NTDs account for a significant and unfairly distributed global disease burden, cost-effective interventions exist to reduce that burden, these interventions are affordable, and they are good investments in universal health coverage and social protection. It builds on the second edition of the *Disease Control Priorities (DCP2)* project (Hotez and others 2006) with new data and analysis. It also takes into account new strategies and tools that have been introduced since 2006 and the increasingly ambitious elimination and eradication targets for individual diseases that have emerged since 2012, including the unprecedented donation by the pharmaceutical industry under the London Declaration of more than a billion medicines annually to treat nine of the most important NTDs. Finally, it helps provide a longer-term perspective on SDG target 3.3 and the 2030 goals.

This chapter is structured around three key NTD interventions, rather than individual NTDs, in recognition of the increasingly integrated delivery of interventions to the poorest, most remote, and otherwise most marginalized communities of the world. These interventions are as follows:

- Preventive chemotherapy by mass drug administration
- Innovative and intensified disease management
- Vector ecology and management.

For simplicity of analysis, we focus on a subset of the NTDs recognized by the WHO. We do not provide a full analysis of veterinary public health interventions against zoonotic NTDs or of water, sanitation, and hygiene (WASH). These conditions are beyond the scope of this chapter, but WASH is addressed in chapter 9 in volume 7 of the third edition of *Disease Control Priorities* (Hutton and Chase 2017). Chapter 13 in volume 8 (Bundy and others 2017) discusses mass deworming programs, and chapter 29 (Ahuja and others 2017) in volume 8 analyzes the economics of such programs.

BURDEN OF NTDs

The MDGs evolved around HIV/AIDS, malaria, and tuberculosis (TB); other diseases were overlooked and not prioritized for funding. The focus was on mortality. These three diseases accounted for about 3.9 million deaths in 2000, including about 875,000 for malaria; NTDs accounted for about 242,000 deaths (Horton 2012; Hotez and others 2014). Several of the NTDs do not kill; they do,

Table 17.1 Global Targets for Control, Elimination, and Eradication toward “the End of NTDs”

Indicator	Target
Incidence/prevalence ^a	<ul style="list-style-type: none"> • Eradication of Guinea worm disease (2015^b) and yaws (2020) • Global elimination of leprosy (2020), lymphatic filariasis (2020), trachoma (2020), onchocerciasis (2025), and human African trypanosomiasis (2020, with zero incidence in 2030) • Regional elimination of schistosomiasis (2020), rabies (2020), and visceral leishmaniasis (2020) • Regional interruption of intradomestic transmission of Chagas disease (2020) • 25 percent reduction in the number of cases of dengue (2020, compared with 2010)
Mortality	<ul style="list-style-type: none"> • 50 percent reduction in number of deaths attributable to dengue (2020, compared with 2010)
Coverage ^a	<ul style="list-style-type: none"> • 75 percent coverage with preventive chemotherapy for food-borne trematode infections and soil-transmitted helminthiasis (2020) • 70 percent of all cases of Buruli ulcer detected and treated (2020) • Universal coverage against NTDs^c (2030)

Source: WHO 2012.

Note: NTDs = neglected tropical diseases.

a. Reaching the incidence and coverage targets should result in at least a 90 percent reduction in the number of people requiring interventions against NTDs between 2015 and 2030; this is the combined NTD indicator that will be monitored under Sustainable Development Goal target 3.3.

b. Target year for Guinea worm eradication has not been updated; only 22 cases were reported in 2015.

c. 80 percent service coverage and 100 percent financial protection of people requiring at least one of five key interventions against NTDs: preventive chemotherapy; innovative and intensified disease management; vector ecology and management; veterinary public health: water, sanitation, and hygiene.

however, disable, disfigure, and even impair the cognitive development of children. Today, the focus of the SDGs has broadened to include healthy lives and well-being for all at all ages.

The disability-adjusted life year (DALY) is meant to account for years of life lost because of premature death, as well as years of life lived with disability. In practice, it tends to underestimate the burden of NTDs in part because of gaps in the data from low- and middle-income countries (LMICs). Even so, in 2012, the NTDs accounted for approximately 22 million DALYs globally, which amounts to about 40 percent of the DALYs for malaria and about 1 percent of the global total. The contribution of individual NTDs to the total is shown in table 17.2.

This burden is heavy, especially for regions and countries where NTDs are most endemic. In several countries in Sub-Saharan Africa, NTDs make up more than 6 percent of the total burden of disease.

However, the NTDs are not only a concern of low-income countries (LICs) in Sub-Saharan Africa. A significant burden is shouldered by the poorest and most marginalized communities of middle-income countries, as evidenced by figure 17.1. Indeed, environmental change and population movement have redefined

tropical diseases. Dengue has reemerged in high-income countries that had not seen cases in decades. Chagas disease now affects migrant populations across North America and Europe. Today, a majority of the poor lives in countries assessed as middle income or above.

With national income and other secular trends being generally upward in the LMICs where NTDs are most prevalent, the overall burden of disease has been coming down since at least 2000. However, the persistence of NTDs in middle- and even high-income countries indicates that some communities have been left behind by the macroeconomic development of the past decades. A review found that more than 60 percent of studies reveal inequalities in the prevalence of NTDs across socioeconomic groups (Houweling and others 2016). For example, in rural Nigeria, the prevalence of ascariasis among children ranges from 10 percent when both parents have at least primary education, to 31 percent when only the mother does, 53 percent when only the father does, and 96 percent when neither parent does (Ugbomoiko and others 2009).

In Ethiopia, trichiasis cases (a consequence of trachoma) are more likely to occur in poorer households, whether measured by asset ownership,

Table 17.2 Disease Burden (Mortality and Morbidity) of Malaria and NTDs, 2012

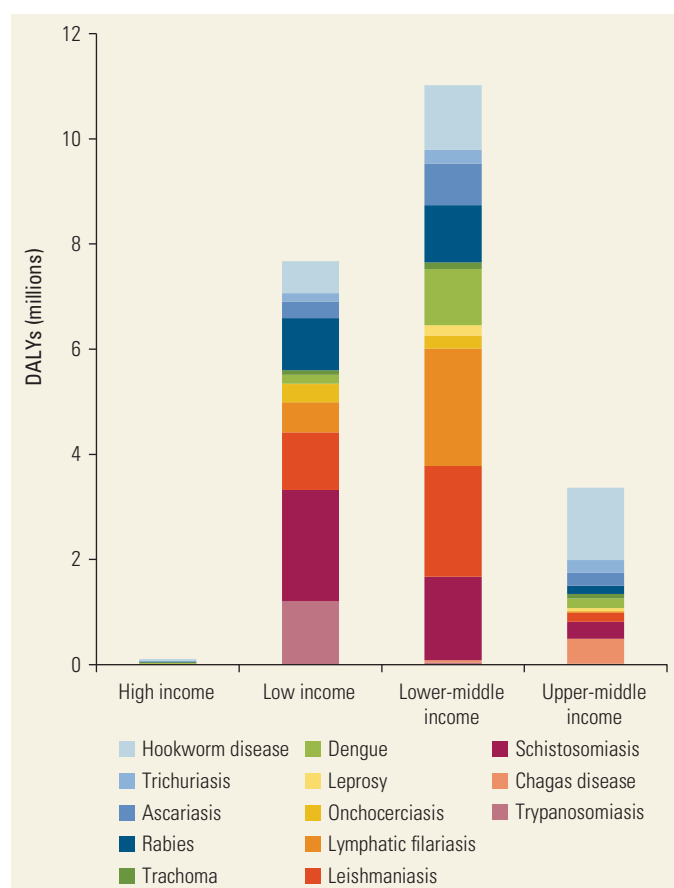
	DALYs (thousands)	%	YLD (thousands)	%	YLL (thousands)	%
Parasitic and vector diseases	72,006	2.62	11,697	1.58	60,309	3.01
Malaria	55,111	2.01	4,301	0.58	50,810	2.54
Trypanosomiasis	1,264	0.05	9	0.00	1,256	0.06
Chagas disease	528	0.02	326	0.04	202	0.01
Schistosomiasis	4,026	0.15	3,179	0.43	848	0.04
Leishmaniasis	3,374	0.12	128	0.02	3,245	0.16
Lymphatic filariasis	2,839	0.10	2,839	0.38	0	0.00
Onchocerciasis	598	0.02	598	0.08	0	0.00
Leprosy ^a	257	0.01	6	0.00	251	0.01
Dengue	1,445	0.05	12	0.00	1,432	0.07
Trachoma	299	0.01	299	0.04	0	0.00
Rabies	2,265	0.08	0	0.00	2,265	0.11
Intestinal nematode infections	5,266	0.19	5,057	0.68	209	0.01
Ascariasis	1,355	0.05	1,146	0.15	209	0.01
Trichuriasis	666	0.02	666	0.09	0	0.00
Hookworm disease	3,246	0.12	3,246	0.44	0	0.00
Total excluding malaria	22,161	0.81	12,453	1.68	9,708	0.48

Source: World Health Organization, http://www.who.int/healthinfo/global_burden_disease/estimates/en/index2.html.

Note: NTDs = neglected tropical diseases. Cause-specific disability-adjusted life year (DALYs), years of life lost (YLLs), and years lived with disability (YLDs). Percentages are expressed relative to the global total.

a. Leprosy is formally not a parasitic disease, it is caused by a mycobacterium. Furthermore, we suspect that the YLD and YLL numbers for leprosy may have been inverted; we nonetheless report them here as in the original source.

Figure 17.1 Disease Burden of NTDs, by Country Income Group, 2012



Source: WHO 2014a.

Note: DALYs = disability-adjusted life years; NTDs = neglected tropical diseases.

Table 17.3 Economic Burden (Lost Productivity) of Selected NTDs

NTD	Sequela	Annualized loss in productive input (%) ^a
Chagas disease	General (excluding severe heart failure)	2–5
Leprosy	Disfigurement	28
Lymphatic filariasis	Hydrocele	14–19
	Lymphedema	2–23
Onchocerciasis	Visual impairment	14–38
	Blindness	79–100
Schistosomiasis	General	1–23
Soil-transmitted helminthiasis	Anemia	0.1–6.0
Trachoma	Visual impairment	25
	Blindness	60–100
Visceral leishmaniasis	General (treated)	6–30

Sources: Ibe and others 2015; Lenk and others 2016.

Note: NTD = neglected tropical disease.

a. Minimum and maximum from the available literature.

self-rated wealth, or peer-rated wealth (the odds range from 2.8 to 8.2) (Habtamu and others 2015). Compared with controls, those with trichiasis are also significantly less likely to participate in economically productive activities, more likely to report difficulty in performing activities, and more likely to receive assistance in performing productive activities (Habtamu and others 2015).

In addition to the disease burden is the heavy economic burden that NTDs impose on patients and their families. Most of the economic cost comes in lost productivity, usually working time (and wages), but also agricultural land, lost to morbidity and disability. The extent of loss of productive inputs depends on the type and severity of the NTD as well as where it occurs (table 17.3). The particularly high economic cost of blindness motivated the World Bank's first investments in health, with the creation of the Onchocerciasis Control Programme in West Africa in 1975.

Added to the productivity losses are the direct medical costs of diagnosis and treatment and, even if tests and medicines are offered free of charge, direct nonmedical costs associated with accessing or adhering to treatment. The latter include transportation, accommodation, and food. Altogether, costs can easily exceed 20 percent of annual household income, a threshold for so-called catastrophic cost that can propel a previously stable household into penury and unsupportable debt (Ruan and others 2016). Protection against this risk requires further public sector investment in finding cases early, treating patients free of charge, and, as required, other social protection to cover transport and other nonmedical and indirect costs. These are some well-documented examples:

Buruli ulcer. In Cameroon, the cost of hospitalization attributable to Buruli ulcer (caused by *Mycobacterium ulcerans*) has been estimated to be 25 percent of household annual earnings, despite treatment being available free of charge. In Ghana, medical costs made up less than 4 percent of total direct costs; the largest cost (81 percent of direct costs) is transportation to treatment (WHO 2015b).

Chagas disease. The cost of Chagas disease (caused by *Trypanosoma cruzi*) was estimated in 2013 to be about US\$7 billion per year, including lost productivity (Lee and others 2013). Health care costs accounted for slightly less than 9 percent of this total. The cost of treatment ranges from less than US\$200 to more than US\$30,000 per person per year in endemic countries, and exceeds US\$40,000 in the United States (WHO 2015b).

Dengue. In Cambodia and Vietnam, “between half and two-thirds of affected households have incurred

debt as a result of treatment for dengue” (WHO 2015b, 82). The economic burden of the disease is measured in the billions of dollars annually; urbanization and climate change are conspiring to raise the cost even higher (Constenla, Garcia, and Lefcourt 2015; Martelli and others 2015; Shepard, Undurraga, and Halasa 2013; Shepard and others 2011; Shepard and others 2014; Undurraga and others 2015).

Human African trypanosomiasis. In the Democratic Republic of Congo, the cost to affected households in a typical rural community represents more than 40 percent of annual household income. New and more effective melarsoprol-free treatment has increased the average cost to treat one patient with second-stage gambiense sleeping sickness from US\$30 in 2001 to US\$440 in 2010 (WHO 2015b).

Leprosy. Erythema nodosum leprosum is a common immune-mediated complication of leprosy. In a district of West Bengal, India, the total household cost of erythema nodosum leprosum was about 28 percent of monthly household income (Chandler and others 2015). Direct costs accounted for 35 percent of this total. Total household costs exceeded 40 percent of household income for more than one-third of cases.

Visceral leishmaniasis. In Bihar, India, 83 percent of affected households belong to the two lowest wealth quintiles (the poorest 40 percent) (Boelaert and others 2009). In Bangladesh, India, Nepal, and Sudan, 25 percent to 75 percent of affected households experience some type of financial catastrophe in obtaining a diagnosis and treatment, even when tests and medicines are provided free of charge (Anoop and others 2006; Meheus and others 2013; Ozaki and others 2011; Sundar and others 2010; Uranw and others 2013).

In addition to the health (death and disability) and economic burden, there is also the social and psychological (mental health) burden of NTDs because of stigma. Reasons given for stigmatization include appearance, fear of contagion, burden on family, hereditary etiology, promiscuity, and performance impediment. This burden is harder to quantify, but there is evidence that no less than 10 NTDs are associated with stigma, with especially strong evidence related to leprosy, lymphatic filariasis, Buruli ulcer, onchocerciasis, and leishmaniasis (Hofstra and van Brakel 2016). The visible impact of NTDs has been shown to be an important determinant of stigma; disease management should therefore have a positive effect on stigma.

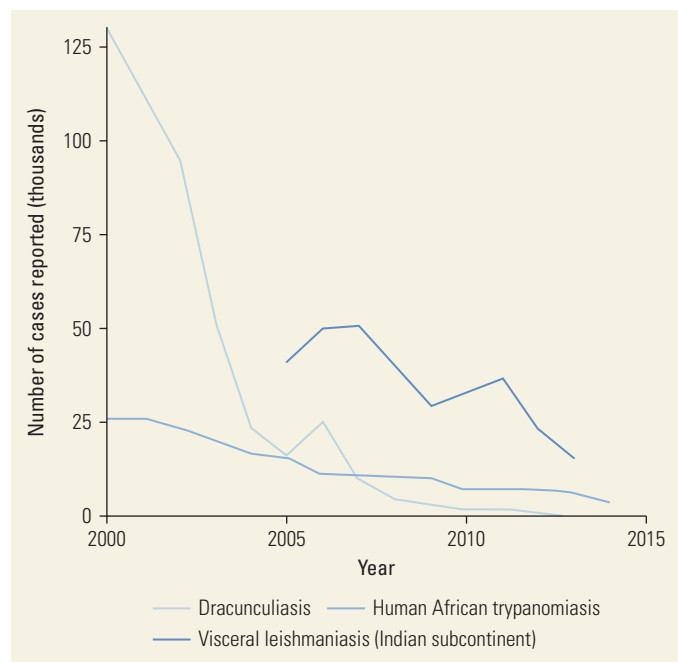
PROOF OF CONCEPT FOR ENDING NTDs

Despite being sidelined in the MDGs, an integrated approach to the prevention and control of NTDs began to take shape during the MDG era, and by the end, NTD interventions had delivered a number of successes. These successes include a reduction of 80 percent in new human African trypanosomiasis (HAT) cases between 2000 and 2014, to an estimated less than 4,000 cases; and a reduction of 75 percent in the number of cases of visceral leishmaniasis (kala-azar) in Bangladesh, India, and Nepal between 2005 (when a regional program was launched) and 2014, to a reported 10,209 cases. In 2000, there were more than 130,000 cases of dracunculiasis (Guinea worm); in 2015, there were only 22 reported cases, reflecting near-eradication (figure 17.2). Map 17.1 shows the reported numbers of cases of these three NTDs targeted for elimination or eradication.

For other NTDs, especially those for which cases are not routinely reported to the WHO, country-level progress has been made toward the interruption of transmission. For example, by 2014, 18 countries reported having been able to stop preventive chemotherapy for lymphatic filariasis, and 8 countries have stopped mass antibiotic treatment for trachoma, because the set targets had been reached.

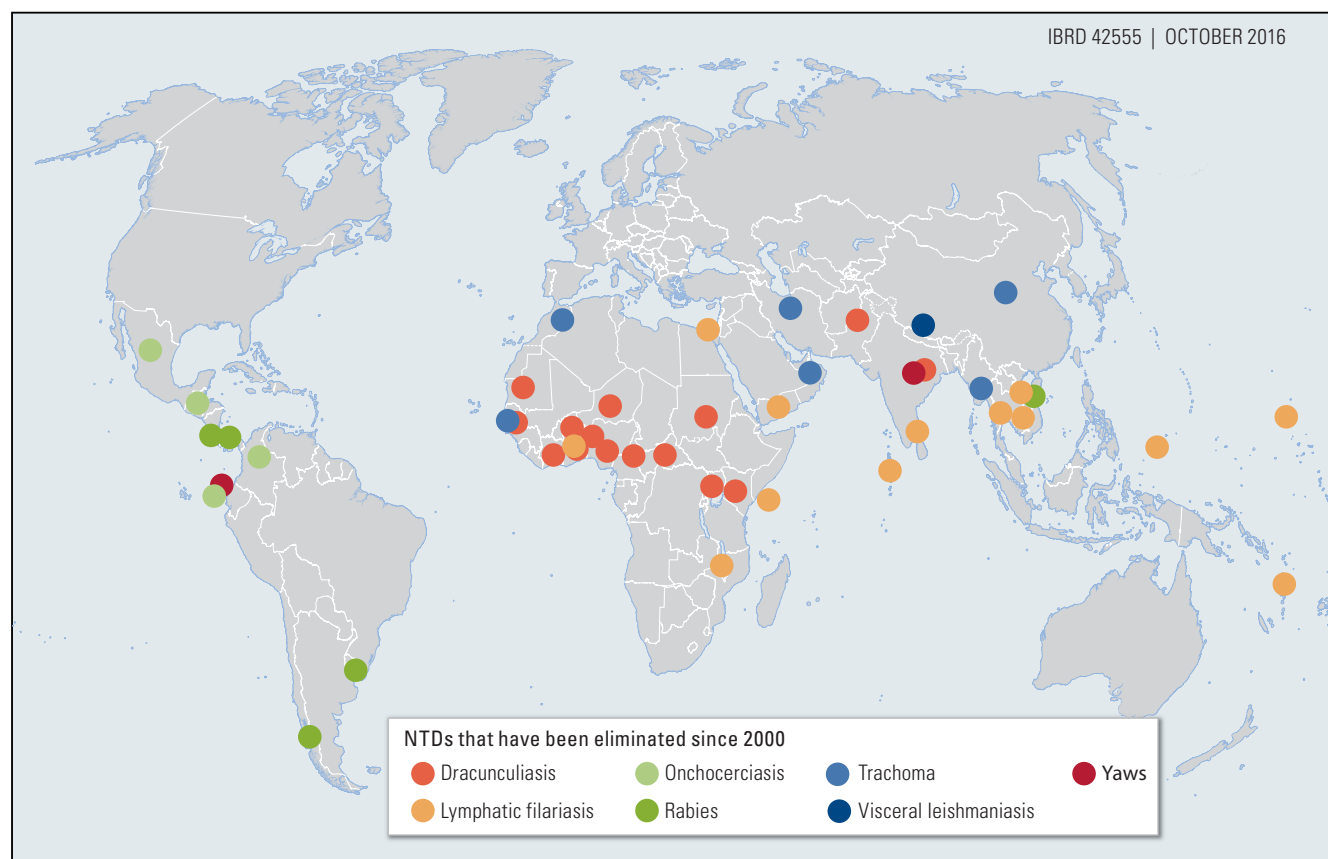
Other NTDs that have been eliminated in certain countries or that are under surveillance for verification

Figure 17.2 Reported Number of Cases of Three Neglected Tropical Diseases Targeted for Elimination or Eradication, 2000–15



Source: WHO Global Health Observatory, (<http://apps.who.int/gho/data/node.main.A1629?lang=en>).

Map 17.1 Countries in Which One or More NTDs Have Been Eliminated or Are under Surveillance for Verification of Elimination, since 2000



Source: WHO Global Health Observatory, (<http://apps.who.int/gho/data/node.main.A1629?lang=en>).

Note: NTD = neglected tropical disease.

of elimination are illustrated in figure 17.3. Those countries are already reaping the economic and financial rewards that come with having eliminated a disease and stopping treatment, thereby freeing up resources for other public health priorities.

Progress on NTD-related mortality includes a reduction in deaths caused by visceral leishmaniasis, rabies, schistosomiasis, HAT, Chagas disease, and soil-transmitted helminthiasis (that is, ascariasis, collectively estimated to be 142,000 deaths in 2012, down from about 220,000 in 2000 (WHO 2014a).

Much of the burden of NTDs occurs in morbidity rather than mortality, and here, too, the progress has been good, albeit somewhat less dramatic, with a decrease of 19 percent in the total number of DALYs between 2000 and 2012, from 1 percent of the global burden of disease to 0.8 percent (WHO 2014a). There have been logistical challenges, of course, that have differed greatly between diseases and between countries. However, elimination of dracunculiasis, for example, has been achieved in some of the most difficult settings in the world.

INTERVENTIONS TO END NTDs

The WHO recommends five interventions for the control, elimination, and eradication of the NTDs: preventive chemotherapy by mass drug administration; innovative and intensified disease management; vector ecology and management; veterinary public health services; and the provision of safe water, sanitation, and hygiene (WHO 2010; see the discussion in volume 7 of this series [Hutton and Chase 2017]). We review the evidence for all but the last two of these interventions.

Delivering Large-Scale Preventive Treatment to Entire Communities

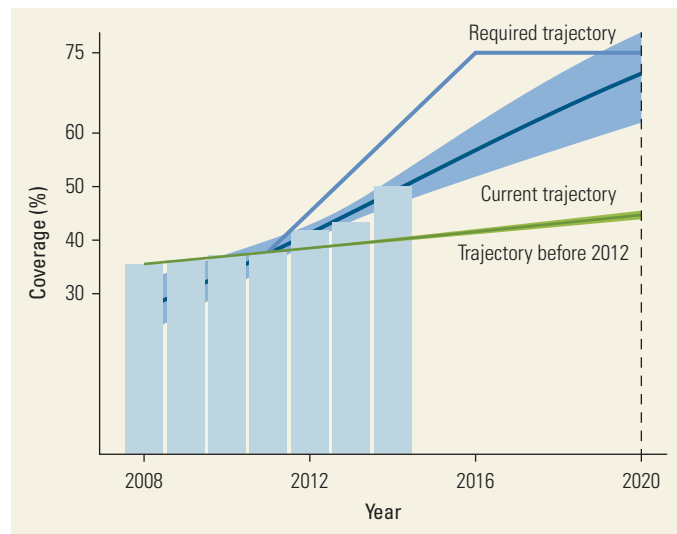
Preventive chemotherapy involves the large-scale delivery of medicines to eligible populations at regular intervals. Medicines donated to and distributed through the WHO are quality assured and safe for administration by non-health workers. Table 17.4 provides the disease-specific

details of how preventive chemotherapy is delivered. In many areas, these diseases do not occur exclusive of each other, but are co-endemic. A combination of medicines is recommended in this scenario. Integrated delivery of treatments for more than one disease is now the norm in several countries, with resulting cost savings (WHO 2015b).

Preventive chemotherapy is effective toward elimination only if the threshold coverage is sustained annually for at least three years or longer, depending on the disease. The WHO has set clear thresholds for effective program coverage, by disease (table 17.4), meaning delivery of medicines to a minimum percentage of eligible individuals during approximately the same time period, with 100 percent geographic coverage of endemic areas. If the threshold coverage is not met, the disease burden is reduced but will return when preventive chemotherapy is stopped. If threshold coverage is met, countries can stop mass treatment, or at least reduce its frequency, and shift resources to integrated disease surveillance and other public health priorities.

The global population in need of preventive chemotherapy is reported to be 1.7 billion as of 2014, of which 851 million people actually received treatment, leaving a coverage gap of approximately 50 percent (WHO 2015c).

Figure 17.3 Update on the Global Status of Implementation of Preventive Chemotherapy, 2008–20



Source: WHO (http://www.who.int/neglected_diseases/preventive_chemotherapy/PC_Update.pdf?ua=1).
Note: Analysis includes current and projected percentage of people receiving preventive chemotherapy for at least one of these diseases (including lymphatic filariasis, onchocerciasis, schistosomiasis, and soil-transmitted helminthiasis) out of the estimated number of people requiring preventive chemotherapy. The required trajectory assumes a linear scale-up to 75 percent, the minimum target coverage indicated in table 17.4.

Table 17.4 Selected NTDs Targeted by Preventive Chemotherapy

Disease	Causative organism and transmission	Medicine, single dose	Target population (minimum effective coverage)	Frequency and duration of intervention
Lymphatic filariasis	Parasites (<i>Wuchereria bancrofti</i> , <i>Brugia malayi</i> , <i>Brugia timori</i>) transmitted by mosquito	Albendazole 400 mg with ivermectin (150–200 µg/kg) or with diethylcarbamazine 6 mg/kg	Ivermectin: ≥ age 5 years Diethylcarbamazine: ≥ age 2 years (65%)	Annually for at least 5 years
Onchocerciasis	Parasites (<i>Onchocerca volvulus</i>) transmitted by blackfly	Ivermectin 150 µg/kg or mcg/kg	> age 5 years (80%) ^c	Annually for at least 10–15 years
Schistosomiasis	People are infected by parasites (<i>S. haematobium</i> , <i>S. mansoni</i> , <i>S. japonicum</i>) when exposed to freshwater infested by cercariae released by intermediate host snails.	Praziquantel 40 mg/kg	SAC (ages 5–14 years) and adults at risk (75%)	Once a year, or every two to three years, depending on community prevalence, for variable or unknown duration ^a
Soil-transmitted helminthiasis	The main parasites that infect people are the roundworm (<i>Ascaris lumbricoides</i>), the whipworm (<i>Trichuris trichiura</i>) and the hookworms (<i>Necator americanus</i> and <i>Ancylostoma duodenale</i>)	Albendazole 400 mg Mebendazole 500 mg	Pre-SAC (< age 5 years) and SAC (age 5–14 years) (75%)	Once or twice a year depending on community prevalence, for variable or unknown duration ^a
Trachoma	Bacterial infection (<i>Chlamydia trachomatis</i>) through contact with infected people or spread by flies	Azithromycin 20 mg/kg to a maximum of 1g (This is given as part of a SAFE ^b strategy)	> age 6 months (80%)	Annually, with the number of rounds given before review dependent on the prevalence of disease at last estimate

Source: WHO (http://apps.who.int/iris/bitstream/10665/43545/1/9241547103_eng.pdf).

Note: g = gram; kg = kilograms; mg = milligrams; SAC = school-age children; µg or mcg = micrograms.

a. Treatment is geared toward reducing the intensity of infection in individuals. The frequency of treatment may be reduced over time, but ultimately, the duration will depend on improved water, sanitation, and hygiene.

b. SAFE strategy comprises: S-eyelid surgery for trichiasis, A-antibiotics, F- facial cleanliness, and E-environmental improvement.

c. 80% of the eligible population is roughly equivalent to 65% of the total population.

Still, it is important to acknowledge the tremendous progress that has been made in shifting the trajectory in coverage up from the levels of 2000–11 (figure 17.3). In 2012, the WHO NTD Roadmap (WHO 2012) and subsequent London Declaration drove the pivot from the trajectory in 2011 (green line) to the current trajectory (dark blue line). It also remains clear that the current trajectory is not sufficient to meet the required level of coverage of 75 percent (light blue line) early enough (2016) to ensure that treatment can be stopped or its frequency reduced by 2020 (WHO 2012).

Morbidity management and disability prevention is a related intervention for those for whom preventive chemotherapy has arrived too late, particularly for those with a long history of infection with lymphatic filariasis or trachoma, now suffering the chronic consequences. Adult filarial worms lodge in the lymphatic system and disrupt the immune system, resulting in swelling of the scrotum and lower limbs. Repeated reinfection with *Chlamydia trachomatis* gives rise to trichiasis, in which eyelashes rub on the eyeball, leading to corneal opacification and blindness. Hydrocele and trichiasis surgery, as well as lymphedema management, are complementary to measures to reduce infection prevalence—the benefits being more visible than those from the distribution of drugs.

The pharmaceutical industry has expressed its commitment to meet medicine requirements. A full list of medicines donated by the pharmaceutical industry is available in annex 5 of the third global report on NTDs (WHO 2015b). These are highly effective medicines—most of which are on the WHO’s list of essential medicines—being provided for free. Logistic constraints have, however, hindered the ability of NTD programs to ensure universal access to these medicines. The delivery

network has been heavily subsidized by communities. Members are selected as community drug distributors and paid in kind or with cash incentives by their communities. This approach has worked well in small-scale projects, but many communities are overstretched. Bridging the coverage gap will require investment in delivery chains within endemic countries; how much is needed and what the return will be are described later in the chapter.

Preventing the Transmission of NTDs by Vectors

Vectors are living organisms that can transmit infectious diseases between humans or from animals to humans (and vice versa). Many of these vectors are bloodsucking insects that ingest disease-producing microorganisms during a blood meal from an infected host (human or animal) and later inject it into a new host during their subsequent blood meal. Mosquitoes are the best known vector, transmitting malaria as well as lymphatic filariasis. Others include blackflies (onchocerciasis), sandflies (leishmaniasis), and triatomine bugs (Chagas disease).

Vector ecology and management aims to control the transmission of the causative pathogens of insect-borne NTDs with proven interventions that are applied in an ecologically friendly manner. The WHO’s integrated vector management strategy has found use in areas with multiple vector-borne diseases or where preventive chemotherapy is contraindicated because of the risk of severe adverse events (for example, in areas of onchocerciasis and *Loa* co-endemicity) and where there is no other intervention to control infection (for example, dengue, chikungunya). NTDs targeted primarily by vector management are listed in table 17.5.

Table 17.5 Selected NTDs Targeted by Vector Ecology and Management Interventions

Disease (vector)	Description of vector management intervention
Chagas disease (hematophagous triatomine or “kissing bug”)	Spray homes and surroundings with residual insecticides Improve walls and roofs of dwellings Use bednets and other personal control measures
Dengue, chikungunya (female mosquitos <i>Aedes aegypti</i> and <i>Aedes albopictus</i>)	Individual and household protection Vector surveillance Biological, chemical, and environmental control (including insecticides) Outbreak preparedness and response
Visceral leishmaniasis or kala-azar (female sandflies)	In areas of the Indian subcontinent where vector control is not already being undertaken by malaria programs: Vector surveillance Indoor residual spraying and use of bednets

Note: NTDs = neglected tropical diseases. Vector control interventions also exist for onchocerciasis, human African trypanosomiasis, and lymphatic filariasis; however, these are not discussed here. There is little recent evidence on their cost-effectiveness or, in the case of lymphatic filariasis, evidence is limited to areas that are co-endemic with malaria.

Coverage with vector management for the prevention of Chagas disease and dengue remains uneven. More than 100 million people still require an attack phase of vector control for the interruption of intradomiciliary transmission of Chagas disease in Latin America. This intensive phase involves residual insecticide spraying by specialized mobile teams two times with a six-month intermediate period (to kill all insects, including the ones coming from eggs) and dwelling or house hygiene and improvement (plastering) to avoid reinfestation.

Although 2 billion to 4 billion people are at risk of dengue or chikungunya, only a handful of counties offer coverage with sustained vector management involving biological, environmental, and chemical measures adapted to the needs of the communities. Most countries only respond to dengue outbreaks when it is too late to make much of a difference (Stahl and others 2013). However, sustained vector control interventions could make a very large difference, not only for dengue and chikungunya, but also for other diseases transmitted by *Aedes aegypti* and *Aedes albopictus*.

Progress toward elimination of visceral leishmaniasis as a public health problem on the Indian subcontinent provides evidence of the impact that vector management can have. In 2005, the governments of Bangladesh, India,

and Nepal launched a comprehensive strategy including integrated vector management. In Nepal elimination has been achieved in 12 districts. In Bangladesh, the number of hyperendemic subdistricts (*upazilas*) decreased from eight in 2012 to two in 2014, with elimination achieved in about 90 percent of endemic upazilas (WHO 2015d).

Providing Treatment and Care to Individuals

Not all NTD cases can be prevented by preventive chemotherapy and vector management, for example, because the drugs are too toxic. A complementary approach focuses on the innovative and intensified clinical management of diseases. Innovation and intensification refer to a shift from passive management to active surveillance, early diagnosis, and treatment, with the aim to eliminate or control, not just to manage. Treatment of Buruli ulcer, for example, has evolved from late-stage surgical removal of infected or dead tissue and correction of deformity to the early-stage use of antibiotics (a combination of rifampicin and streptomycin or amikacin). The gains go beyond health benefits to include reductions in the cost of hospitalization to health systems and to individuals. The NTDs for which the primary intervention is disease management are listed in table 17.6.

Table 17.6 Selected NTDs Targeted by Disease Management Interventions

Disease (agent)	Disease management intervention
Buruli ulcer (<i>Mycobacterium ulcerans</i>)	Early case detection and antibiotic treatment, including rifampicin and streptomycin, or rifampicin and clarithromycin Surgical removal of dead skin and grafting Rehabilitation for deformities
Chagas disease (<i>Trypanosoma cruzi</i>)	Early case detection and treatment with nifurtimox and benznidazole Adequate screening of blood for transfusion Screening (testing) of organ, tissue, or cell donors and receivers Screening of newborns and other children of infected mothers to provide early diagnosis and treatment Other morbidity-specific treatment
Human African trypanosomiasis (<i>Trypanosoma</i>)	Early case detection and treatment with pentamidine or suramin or nifurtimox-eflornithine combination treatment (NECT), depending on the stage of the disease
Leishmaniasis (<i>Leishmania spp</i>)	Early case detection For visceral leishmaniasis, treatment options include: sodium stibogluconate, meglumine antimonite, paromomycin, liposomal amphotericin B or miltefosine, depending on the parasite species and the endemic region For cutaneous leishmaniasis, management options include local or systemic treatments with antileishmanial drugs or local procedures with cryotherapy, thermotherapy
Leprosy (<i>Mycobacterium leprae</i>)	Early case detection and treatment with multidrug regimen (combination of rifampicin, dapsone, and clofazimine) and management of morbidity and prevention of disability
Yaws (<i>Treponema pallidum pertenue</i>)	Formerly, identification of the population at risk of infection by case finding (active and passive) and treatment with injectable penicillin Currently, Total Community Treatment followed by Total Targeted Treatment of confirmed cases and their contacts with single dose of azithromycin

Note: NTDs = neglected tropical diseases.

The inclusion here of yaws warrants an explanation, given the recent shift in strategy from individual treatment with injectable penicillin to mass treatment with single-dose azithromycin. While the risk is thought to be low in populations with little previous antibiotic exposure, surveillance is undertaken to guard against antimicrobial resistance. This mass treatment for yaws is similar to preventive chemotherapy but is known as Total Community Treatment. In keeping with the convention within the NTD community, this chapter considers Total Community Treatment as separate from preventive chemotherapy.

COST AND COST-EFFECTIVENESS OF INTERVENTIONS TO END NTDS

This section is a synthesis and update of the review of the cost and cost-effectiveness conducted for the WHO's NTD report (WHO 2015b) and subsequent systematic reviews.

Preventive Chemotherapy

Unit Cost of Delivery

Advocacy around preventive chemotherapy has typically put the cost per person treated at less than US\$0.50. While useful for advocacy, the focus on a single number misrepresents the complexity of delivering “free” donated medicines to more than 1 billion people across the world.

There is now a rich literature—34 studies of 23 countries and at least 91 sites over 19 years—documenting the cost per person treated in diverse settings (Fitzpatrick and others, forthcoming). The average unit cost is US\$0.40 (in 2015 U.S. dollars) in financial terms, but the average unit cost increases to US\$0.70 in studies that also consider the economic cost of ministry of health staff time and assets. About half of the available estimates of the economic unit cost fall between US\$0.30 and US\$1.00, but they range from a low of US\$0.02 in large-scale programs to US\$2.9 in smaller projects. Benchmarking tools can help assess the value for money in mass treatment campaigns (WHO 2015b).

Cost-Effectiveness

Hotez and others (2006) described preventive chemotherapy as one of the most cost-effective interventions available in public health. The large and unprecedented donation of NTD medicines in the London Declaration in 2012 strengthens that case from the perspective of national health systems. Indeed, reviews continue to show that preventive chemotherapy remains cost-effective, even with an expansion beyond the traditional zones of focus, or with an increase in treatment frequency to accelerate progress (Keating and others 2014).

Some of the more recent cost-effectiveness analyses are presented in table 17.7, with results standardized for prices in 2012.

Table 17.7 Recent Cost-Effectiveness Analyses of Preventive Chemotherapy

Disease	Study	Intervention	Setting	Target population	2012 US\$ per DALY averted, relative to doing nothing
Lymphatic filariasis	Turner and others 2016	Albendazole + ivermectin	Global	All	28 ^a
Onchocerciasis	Turner and others 2014	Ivermectin, annual	Africa	Mesoendemic (microfilarial prevalence: 40%)	15
				Hyperendemic (60%)	6
				Highly hyperendemic (80%)	3
Schistosomiasis and STH	Turner and others 2015	Albendazole + praziquantel	Global	School-age children	5-80
	Lo and others 2015		Côte d'Ivoire	School-age children	114
Trachoma	Baltussen and Smith 2012	Mass treatment with azithromycin + trichiasis surgery	Sub-Saharan Africa	95% coverage	22–83 ^b

Note: DALY = disability-adjusted life year; STH = soil-transmitted helminthiasis.

a. Stone and others (2016) do not report the number of DALYs averted relative to a null (do nothing) scenario; they report the incremental costs and effects of a hypothetical eradication program over the baseline elimination program.

b. This estimate is based on Baltussen and Smith (2012) using median purchasing-power-parity exchange rates for Sub-Saharan Africa in 2012 to convert from international dollars of 2000. Baltussen and Smith (2012) used 2012 market prices for azithromycin; an assumption of zero cost would be closer to the reality of the current situation. See text for further comment.

Annual mass treatment with ivermectin is estimated to cost 2012 US\$3–US\$15 per DALY averted, depending on the degree of onchocerciasis endemicity; biannual mass treatment would cost an additional 2012 US\$12–US\$36 per DALY averted in hyperendemic areas (Turner and others 2014). This does not take into account the substantial collateral reduction in DALYs attributable to the impact of ivermectin on lymphatic filariasis, soil-transmitted helminthiasis (STH), and scabies (Krotneva and others 2015).

With regard to STH, there has been a recent controversy about the extent to which it is possible to detect population-level benefit from mass treatment. However, there is no doubt that infected persons are at risk of disease and require treatment; the WHO recommendation is for mass treatment in communities where prevalence exceeds 20 percent (see Bundy and others 2017 for a discussion of these issues). A recent review finds that most studies present results within the range of being highly cost-effective according to World Bank thresholds (Turner and others 2015). Mass treatment of school-age children in Côte d'Ivoire for STH and schistosomiasis together costs 2014 US\$118 (2012 US\$114) per DALY averted relative to doing nothing (Lo and others 2015). Mass treatment of the entire community would also be cost-effective, at 2014 US\$167 (2012 US\$161) per DALY averted relative to school-age children only (Lo and others 2015). Combination with other interventions is also possible. Mass treatment for STH costs 2012 US\$13 per DALY averted when added to a vitamin A supplementation campaign for children ages 6 months to 14 years in Uganda (Fiedler and Semakula 2014).

Of the medicines delivered as preventive chemotherapy, azithromycin, a broad-spectrum antibiotic, has the greatest market value. The cost-effectiveness of preventive chemotherapy for trachoma (relative to other interventions for the prevention of blindness) depends crucially on assumptions about the cost of azithromycin. There is no market price for azithromycin for use in global trachoma elimination. Applying the market price of azithromycin for use in smaller-scale programs, mass treatment combined with trichiasis surgery costs about 2012 US\$83 per DALY averted in Sub-Saharan Africa, relative to doing nothing (Baltussen and Smith 2012). In practice, azithromycin is available as a free donation to trachoma-elimination programs worldwide, and the cost per DALY averted is lower than the cost using market pricing. An earlier study suggested a 73 percent decrease in the cost per DALY averted with donated azithromycin (Baltussen and others 2005). Therefore, the cost per DALY averted is probably closer to 2012 US\$22.

All of the cost-effectiveness ratios described above are well below the threshold of one times gross domestic product (GDP) per capita, implying that they are very cost-effective (WHO-CHOICE 2012). Even so, they may be overstated. Integrated delivery of more than one medicine at a time is safe and there is evidence that it will reduce cost (Evans and others 2011; Leslie and others 2013).

Vector Ecology and Management

Chagas Disease

The cost-effectiveness of vector control for Chagas disease in the Argentinean Chaco region has been estimated to be 2004 US\$45–US\$132 per human case averted, depending on the strategy chosen (Vazquez-Prokopec and others 2009). A mixed strategy—vertical (centralized) attack phase followed by a horizontal (community-led) surveillance phase—is thought to be the most cost-effective option. A comparison of vector control policies for Chagas disease in Colombia to a do-nothing policy revealed net benefits for all considered villages at a willingness to pay of 2004 US\$631 (2012 US\$940) per DALY averted (Castillo-Riquelme and others 2008).

Dengue

For dengue, *DCP2* put the cost per DALY averted by vector control at US\$1,992–US\$3,139 (Cattand and others 2006). Since then, the dengue economics literature suggests lower cost-effectiveness ratios that range from 2005 US\$227 (2012 US\$334) per DALY averted by larval control in Cambodia to 2009 US\$615–US\$1,267 (2012 US\$779–US\$1,604) per DALY averted by adult mosquito control in Brazil (Suaya and others 2007; Luz and others 2011). Environmental change, including urbanization and climate change, strengthen the investment case for sustained vector control, which is cost-effective even in the era of a low-cost, medium-efficacy vaccine. If benefits for the control of chikungunya and Zika virus (transmitted by the same vector) were taken into account, the cost per DALY averted would be even lower.

Disease Management

Cutaneous Leishmaniasis

The cost-effectiveness of interventions for cutaneous leishmaniasis was not specifically discussed in *DCP2*. The difficulty with assessing their cost-effectiveness is that this form of the disease is not fatal and disability weights

may not fully reflect the social stigma associated with disfigurement. Nonetheless, recent economic evaluations suggest that interventions for early diagnosis and treatment can be cost-effective, ranging from 2010 US\$156 (2012 US\$218) per DALY averted in Argentina to 2003 US\$1,200 (2012 US\$3,000) per DALY averted by treatment in a complex emergency setting in Afghanistan (Orellano, Vazquez, and Salomon 2013; Reithinger and Coleman 2007).

Visceral Leishmaniasis

Liposomal amphotericin B (AmBisome) has been found to be the most effective treatment option available for the Indian subcontinent for visceral leishmaniasis (Meheus and Boelaert 2010). Recent donations of AmBisome have also made it the most cost-effective treatment option from the health system perspective. In Bangladesh, a comprehensive elimination program involved active case detection, single-dose treatment with donated AmBisome, indoor residual spraying, long-lasting insecticide treated nets, and environmental vector management. It was the most cost-effective option available at thresholds above 50 percent of GDP per capita, and cost far less than 50 percent of GDP per capita per DALY averted relative to doing nothing (Federici and others, forthcoming).

Human African Trypanosomiasis

The latest economic evaluations identified in a recent review focused on the Democratic Republic of Congo and Angola, of which the Democratic Republic of Congo makes up most of the remaining burden of HAT in the world (Sutherland and others 2015). Case detection, diagnosis, and treatment were considered cost-effective at 2002 US\$17 (2012 US\$79) per DALY averted in the Democratic Republic of Congo. However, the current treatment, nifurtimox-eflornithine combination therapy (NECT), has not yet been evaluated for cost-effectiveness. Given that NECT too is donated and has efficacy in excess of 90 percent, we would anticipate at least similar ratios.

Leprosy

For leprosy, DCP2 put the cost per DALY averted by case detection and treatment at less than US\$50 (Remme and others 2006). Since then, the pharmaceutical industry has committed an unlimited number of treatments to overcome the disease. From the health system perspective, therefore, treatment is more cost-effective than ever. The economic evaluation of leprosy elimination programs focuses primarily on the cost-effectiveness of interventions to detect more cases earlier (Ezenduka and others 2012; Idema and others 2010). The challenge is to

deliver those treatments early enough to prevent disability and further transmission.

Yaws

A global yaws eradication campaign could be established with a relatively modest investment in the period to 2020—about 2012 US\$100 million to US\$500 million in 12 endemic countries. Yaws eradication would cost about 2012 US\$26 per year lived without disability or 2012 US\$324 per DALY averted. Global financial support is not yet available in the same proportions as for other NTDs. The cost to the public sector would be significantly reduced by donations of azithromycin for yaws, as is done for trachoma (Fitzpatrick, Asiedu, and Jannin 2014; WHO 2015b).

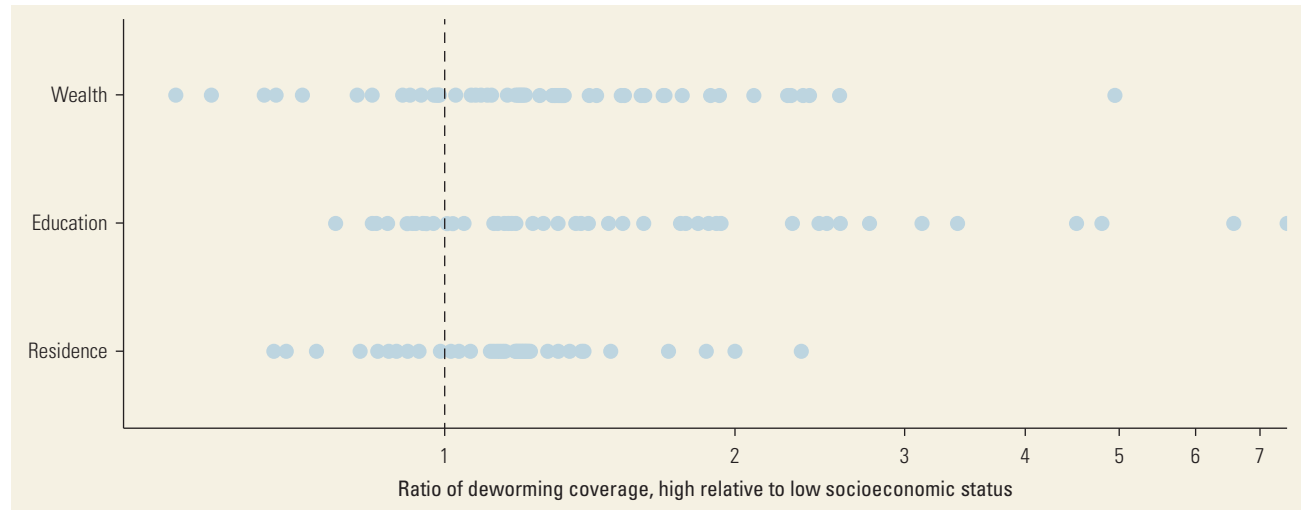
More evidence is needed on the cost-effectiveness of interventions for Buruli ulcer and mycetoma. Such evidence will likely come from evaluations of integrated approaches to screening, diagnosing, and treating these and other skin-related NTDs, especially cutaneous leishmaniasis, leprosy, and yaws.

FAIRNESS OF INTERVENTIONS TO END NTDs

Mass treatment is an intervention that favors women in most countries. NTDs could have a disproportionate impact on the health and well-being of girls and women (including pregnant women) because they negatively affect female reproductive health; exacerbate anemia in women of reproductive age; and increase susceptibility to sexually transmitted infections, including HIV/AIDS. Mass treatment turns out to be quite favorable to women. In coverage surveys from 37 countries from which data were available, the gender ratio (female-to-male) was between 0.96 and 1.17 (Worrell and Mathieu 2012). Data from Uganda also suggest that coverage tends to be higher among females than males (Rilkoff 2013). Men tend to be away from home more often than the women within a household, whether for work or travel.

Inequity persists along other dimensions of socioeconomic status. Disaggregation of NTD intervention coverage is not yet routinely done. The disaggregated data we do have are from household surveys that ask whether children ages 6–59 months had been given deworming medication in the past six months. This is only a subset of the population requiring treatment for one NTD—STH—but it points to both a challenge and an opportunity. In most countries, deworming coverage is similar in both rural and urban areas, but higher among educated and wealthy households who need it least (figure 17.4). A dozen or so countries have demonstrated that higher rates of coverage can be achieved among those who need it most.

Figure 17.4 Deworming Coverage among Children Ages 6–59 Months in 55 Countries, Ratio



Source: Demographic and Health Surveys, most recent available (2006–14) from 55 countries.

Note: Ratio of deworming coverage: Residence shows the ratio of coverage in urban relative to rural areas; Education shows the ratio of coverage among households headed by those with higher relative to no education; and Wealth gives the ratio of coverage among the wealthiest 20 percent relative to the poorest 20 percent of households.

TARGETS FOR THE SCALE-UP OF INTERVENTIONS TO END NTDs

The current improved support for control and elimination of NTDs reflects a well-structured strategy, availability of cost-effective interventions, and a clear road map against which progress can be measured. Endemic countries have adopted global targets and milestones in national NTD master plans. Within these plans the national NTD programs are responsible for ensuring that all donated essential medicines are delivered to all the citizens requiring them.

Treatment Targets

The WHO’s NTD Roadmap (WHO 2012) set clear targets for the eradication or elimination of 11 of the 17 NTDs considered by 2020. Eradication is the “permanent reduction to zero of a specific pathogen, as a result of deliberate efforts, with no more risk of reintroduction,” while elimination (of transmission) is the “reduction to zero of the incidence of infection caused by a specific pathogen in a defined geographical area, with minimal risk of reintroduction, as a result of deliberate efforts; continued actions to prevent re-establishment of transmission may be required” (WHO 2015a, 1). Elimination thresholds are defined differently by disease, but in general involve the reduction of disease impact to below levels of public health importance. SDG target 3.3 is to “end the epidemic” of NTDs. For global monitoring purposes, the existing coverage and

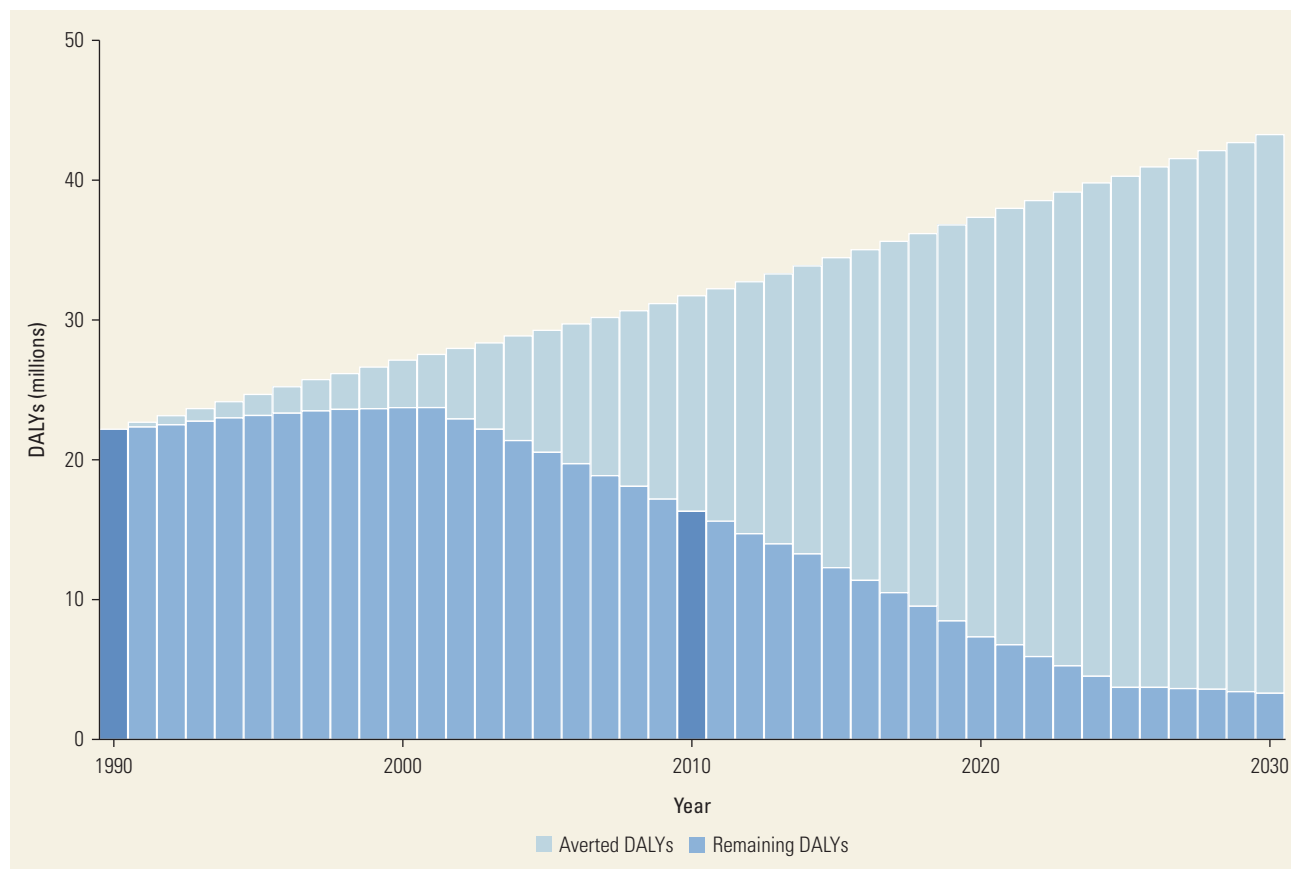
eradication or elimination targets for individual NTDs are being brought together under a single indicator for 2030: reduction in the number of people requiring interventions against NTDs.

This indicator will capture but is not limited to eradication of yaws (2020); global elimination of leprosy (2020), lymphatic filariasis (2020), trachoma (2020), onchocerciasis (2025), and HAT (2020, with zero incidence in 2030); and regional elimination of schistosomiasis (2020) and visceral leishmaniasis (2020). These remain critical milestones on the path toward the end of the NTD epidemic by 2030. If these milestones are met, the total number of people requiring treatment for NTDs may begin to decrease as soon as 2017, as diseases are eradicated, eliminated, and controlled.

Between 2015 and 2030, we should see a 90 percent reduction in the number of people in need of mass and individual treatment globally. The projected 90 percent reduction in the number of people requiring treatment will be associated with a projected 75 percent reduction in DALYs, from 12 million in 2015 to 3 million in 2030, expected from the achievement of NTD Roadmap targets for nine NTDs (figure 17.5). The decrease in the total number of people requiring treatment against NTDs from about 1.6 billion in 2015 to less than 300 million means far less death, disability, and disfigurement; but it also means far less cost to households and to the health system. This is why we speak of spending on these NTDs as an investment.

At the same time, achievement of the 2020 targets and even the end of treatment is not exactly the same as the

Figure 17.5 Health Impact of Achieving the WHO's NTD Roadmap Targets for 2020 and Sustaining Them until the "End of NTDs" by 2030, in Relation to Having Done Nothing, Expressed as a Continuation of the 1990 Situation, Corrected for Demographic Trends



Sources: de Vlas and others 2016; <https://erasmusmcmgz.shinyapps.io/dissemination/>.

Note: DALYs = disability-adjusted life years; NTDs = neglected tropical diseases. These trends are for the nine so-called London Declaration NTDs only, which explains why the total number of DALYs is less than the 22 million DALYs reported in table 17.2 for 2012.

end of NTDs. Rehabilitation and disability inclusion will need to be sustained well beyond 2030 for those people for whom prevention arrived too late and for whom the consequences are irreversible. Vector control for Chagas disease and dengue are interventions that are also likely to extend beyond 2030. To be sustainable, these longer-term services and interventions will need to be included within benefit packages under universal health coverage.

Investment Targets

The third WHO global NTD report set investment targets for reaching the 2020 Roadmap and 2030 SDG targets (WHO 2015b). Including vector control for Chagas disease and dengue, a total of \$18 billion is targeted for the period 2015–30, or about US\$2.1 billion per year. Most of the investment in vector control is required in upper-middle-income countries (UMICs). Excluding vector control,

the investment target for treatment (preventive chemotherapy and individual treatment) is about US\$750 million per year during 2015–20, and about US\$300 million per year during 2020–30. These amounts exclude the value of donated medicines, estimated to be about \$4.5 billion when using the lowest prices negotiated on the market (MSH 2014). An estimated US\$2.8 billion is required to deliver donated medicines to end users either in the form of mass treatment or facility-based care.

Where will this investment come from? Between 2012 and 2014, about \$200 million to \$300 million was disbursed or committed by foreign donors (Uniting to Combat Neglected Tropical Diseases 2014). This is about one-tenth of the investment target in endemic countries. At most, it would cover the investment required in LICs. As reflected in the discourse around the SDGs, the time has come for a shift in focus from foreign donors to domestic investment by governments and stakeholders in

endemic countries. The third WHO global NTD report argued that targets for domestic investment should be set such that the realization of the end of NTDs will not depend disproportionately on foreign aid (WHO 2015b).

In 2011, the domestic share of total expenditure on health was 71 percent in LICs, 98 percent in lower-middle-income countries, and more than 99 percent in UMICs (WHO 2014b). Allowing for an upward trend toward 2030 in line with recent trajectories in economic growth, the domestic share in LICs could rise to 93 percent by 2030 (WHO 2015b). Of course, this average conceals considerable variation between countries. Nonetheless, if recent trajectories in economic growth are maintained, by 2030 the domestic share could exceed 80 percent in all of them (WHO 2015b). We apply these domestic shares to the total investment target for NTDs to obtain domestic investment targets for NTDs.

For all income groups, domestic investment targets for NTDs decrease after 2020 in absolute (dollar) terms as coverage targets are achieved and NTDs are controlled, eliminated, or eradicated. These targets for domestic investment are affordable. The domestic investment target for NTDs represents less than one-tenth of 1 percent of domestic expenditure on health expected within the group of lower-middle-income countries for 2015–30. The percentage is highest for the group of LICs, where the domestic investment target for NTDs is nevertheless still well below 1 percent of domestic expenditure on health.

In many endemic countries, the costs of community-level interventions are borne by endemic communities themselves, who provide the volunteers and incentives. In addition to financing delivery, all levels of government have a critical role in ensuring that nonfinancial barriers to access are also addressed. They can do this by providing waivers and supporting drug logistics through all administrative levels, especially at the very critical level of the community, where delivery occurs.

The end of NTDs is an achievable and affordable SDG target for which endemic countries could take political and financial control. The returns to their poorest citizens will be substantial.

RETURN ON INVESTMENTS TO END NTDs

The health impact of meeting the WHO 2020 targets and the end of NTDs by 2030 has been calculated for nine NTDs (de Vlas and others 2016). Between 2011 and 2030, 600 million DALYs would be averted: 30 million DALYs per year on average (figure 17.5). These health gains include about 150 million irreversible disease manifestations averted (such as blindness) and 5 million averted deaths. Among the preventive-chemotherapy

NTDs, 96 percent of the health gains would be attributed to averted disability, and within the intensified-disease-management NTDs, 95 percent of the impact would be realized from averted deaths.

The impact compares favorably to the total investment of US\$27 billion thought to be required in the period 2011–30 for achievement of global targets for those nine NTDs (our calculations based on abovementioned targets for 2015–30). That investment implies US\$45 per DALY averted or US\$178 per irreversible disease manifestation averted over the same period.

In addition to their impact as measured by DALYs, NTDs are known to cause financial hardship among affected individuals, which can exacerbate the cycle of poverty. A conservative estimate suggests that the end of NTDs would avert a total of international dollars (I\$) 35 billion in out-of-pocket (OOP) health expenditure by affected individuals between 2011 and 2030 (Lenk and others, forthcoming; Redekop and others, forthcoming). This averted cost includes medicines, tests, travel, and food not covered by public providers or by health insurance. It does not capture the additional averted costs of household coping mechanisms, such as indebtedness, or the irreversible consequences of catastrophic health expenditure.

Progress toward the end of NTDs would avert a further I\$622 billion in wages lost by affected individuals between 2011 and 2030. This number does not include the significant long-term benefits of school attendance for employment (Ahuja and others 2015). The choice by the Global Burden of Disease (2010) project (on which the analysis was based) not to include so-called subtle morbidities, such as impaired cognitive development, poor mental health from stigma, and discrimination because of disfigurement, is controversial. The benefit to affected individuals of averted OOP health expenditures and lost wages is therefore conservatively estimated to be I\$657 billion between 2011 and 2030, or an average of I\$33 billion per year.

We convert the benefits reported by Redekop and others (forthcoming) and Lenk and others (forthcoming) from 2010 international dollars to 2015 U.S. dollars for direct comparison to the investment targets described in the previous section.

Of course, some of this benefit is attributable to investments made before 2011. We conservatively assume that investments begun in 1990 were at the level of those in 2011 (in real terms); 1990 is assumed to mark the beginning of concerted global efforts to control most NTDs and 2011 is assumed to mark the beginning of the recent scale-up in investment to eliminate them. In reality, investments before 2011 were probably lower than this in most countries. We do not consider the investments in improved housing and water and sanitation that occurred over the same period; these investments

were not targeted at the NTDs but nonetheless contributed to their control.

We then calculate a rough estimate of the net benefit to affected individuals from 1990 to 2020 (NTD Roadmap targets) and to 2030 (the SDG target). Net benefit per dollar invested is the present value of the benefit to affected individuals minus the present value of the cost to public and philanthropic funders, divided by the present value of the cost to funders. We apply a discount rate of 3 percent per year for both costs and benefits.

The net benefit to affected individuals is US\$17 for every dollar invested by funders during the period 1990–2020 and US\$28 for every dollar invested in the period 1990–2030 (table 17.8). It ranges from US\$8 per dollar invested in Africa to US\$398 per dollar invested in the Western Pacific (including China), and US\$4 per dollar invested in LICs to US\$273 per dollar invested in UMICs.

Taking into account the period during which the investments and returns are to be made, we also calculate an annualized compounded rate of return. The end of NTDs offers a 31 percent rate of return overall. It ranges from 19 percent per year in the Eastern Mediterranean Region to 59 percent in the Western Pacific (including China), and 14 percent in LICs to 54 percent in UMICs.

Lower net benefits and rates of return in LICs are due in large part to the way in which averted productivity losses have been valued, that is, using GDP per capita of the bottom 20 percent of the population of each country. This approach assigns a lower benefit to lower-income and more unequal countries. Good physical health without disability is arguably more important in LICs with large informal sectors that revolve around subsistence. As a result, the numbers are particularly conservative estimates of the net benefit for affected individuals in LICs.

What is clear from even this preliminary analysis is that investment in interventions against NTDs is a fair and efficient investment in social justice. The benefit to affected individuals—the poorest and most marginalized—greatly exceeds the cost to public and philanthropic funders of providing it. If the new social compact articulated at the Addis Ababa Conference on Financing for Development is to involve transfers to the poor (as SDGs 1 and 10 on ending poverty and reducing inequalities suggest that it should), then ending NTDs is an efficient way of making those transfers.

This benefit can be measured by OOP health expenditure and productivity losses averted. It thereby supports two additional targets of the SDGs: universal

Table 17.8 Benefits, Costs, Net Benefits, and Rates of Return on the End of Selected NTDs, Best Estimates

	Benefit to Affected Individuals, 2015 US\$ (billions)		Cost to Funders, 2015 US\$ (billions)		Net Benefit to Affected Individuals per Dollar Invested by Funders		Annualized Compounded Rate of Return (%)	
	2015–2020	2015–2030	2015–2020	2015–2030	1990–2020	1990–2030	1990–2020	1990–2030
Preventive-chemotherapy NTDs ^a	119.7	399.0	2.8	6.2	27.4	42.8	35	35
Disease-management NTDs ^b	5.4	20.9	1.1	2.2	0.9	2.8	11	13
Total	125.1	419.9	3.9	8.4	16.9	28.4	30	31
African Region	9.2	40.6	1.5	3.0	3.0	8.0	18	20
Region of the Americas	5.6	21.9	0.1	0.3	10.2	26.1	24	25
Eastern Mediterranean Region	1.9	8.5	0.2	0.3	3.9	13.0	16	19
European Region	0.1	0.5	<0.1	<0.1	5.1	14.1	19	21
South-East Asian Region	27.1	98.9	1.9	4.5	4.9	10.1	19	21
Western Pacific Region	80.5	246.4	0.2	0.4	260.6	397.7	59	59
Low-income countries	7.5	29.3	1.3	2.5	1.3	4.0	11	14
Lower-middle-income countries	29.2	113.2	2.4	5.3	6.1	12.3	22	23
Upper-middle-income countries	87.6	274.3	0.3	0.5	165.4	272.7	54	54

Sources: Based on Lenk and others 2016; Redekop and others, forthcoming; WHO 2015b.

Note: NTDs = neglected tropical diseases.

a. Integrated delivery of preventive chemotherapy medicines for lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helminthiasis, and trachoma; also includes post-preventive chemotherapy surveillance and morbidity management and disability prevention.

b. Individual management of human African trypanosomiasis (HAT), leprosy, and visceral leishmaniasis (VL); also includes active case finding for HAT, leprosy, and VL, and vector control for VL; includes the cost of integrated disease surveillance in HAT-endemic areas.

health coverage and social protection. Universal health coverage means, among others, financial risk protection against OOP health expenditure. Social protection includes benefits for people of working age in case of disability. As countries struggle with how to finance universal health coverage and social protection, prioritizing interventions to end NTDs can guide countries' first decisive steps on the long path toward those goals. Investment in interventions against NTDs puts progress on universal health coverage within reach of even the weakest health systems.

PLACE OF NTDs IN THE GRAND CONVERGENCE

In 2013, the *Lancet* Commission on Investing in Health addressed the question of whether the world could achieve a grand convergence, in which poorer countries would see their infectious, maternal, and child health outcomes converge with the levels of wealthier nations—through increased investments in health interventions and systems to combat common causes of mortality and morbidity. There are now estimates of what the grand convergence might achieve and what investment would be required by 2030 (Boyle and others 2015).

Those estimates focus on lower-middle-income countries. They consider the costs of scaling up interventions for reproductive, maternal, and child health; and HIV/AIDS, TB, and malaria interventions; as well as the cost of strengthening health systems. They suggest that convergence would avert more than 130 million deaths between 2015 and 2030. The incremental costs of convergence would be about US\$62 billion in 2015, rising to about US\$86 billion in 2030. The end of NTDs is a high-impact and low-cost contribution to the grand convergence.

Convergence in the burden of NTDs would avert about 519 million DALYs in the period 2015–30, including about 5 million deaths or 4 percent of the convergence total of 130 million deaths (de Vlas and others 2016). As table 17.8 shows, the cost in lower-middle-income countries is US\$7.8 billion in 2015–30; this amount is US\$0.5 billion per year or less than 1 percent of the convergence total. The NTDs compare favorably with other major diseases as measured by deaths that could be averted by 2030 and the investment needed. This comparison is favorable even though up to 96 percent of the health gains from convergence in NTDs would be in averted disability rather than death (de Vlas and others 2016). A more inclusive metric of grand convergence would reveal the true contribution of convergence in NTDs.

Convergence in NTDs also stands out in the grand convergence narrative in its sustainability. Whereas the incremental costs of convergence increase from US\$62 billion in 2015 to US\$86 billion in 2030, the costs of convergence in NTDs decrease from US\$750 million per year during 2015–20 to about US\$300 million per year during 2020–30. In this sense, there is a special role for NTDs in leading the way toward the grand convergence through the elimination of infectious diseases targeted by the SDGs.

CONCLUSIONS

The elimination of the NTDs was a late and ad hoc addition to the MDG era, leaving a legacy of 22 million DALYs in 2012, a burden not far behind those of malaria and TB. As we enter the SDG era the world is seeking to rethink this opportunity and look toward the end of NTDs in 2030. The ambitious WHO NTD Roadmap (WHO 2012) and the massive donation of treatments for nine NTDs have built on successes in integrated treatment of multiple diseases in the poorest and most marginalized populations, and contribute to the potential of ending NTDs for as little as US\$3 per DALY averted.

The evidence is clearly in favor of including the following within the package of essential interventions for all low-income endemic countries (based on a cost per DALY averted of 2012 US\$250 or less): preventive chemotherapy for at least five NTDs; comprehensive control (including vector control) for visceral leishmaniasis; and early detection and treatment of cutaneous leishmaniasis, HAT, and leprosy. Other interventions against NTDs should also be included on a country-by-country basis. Populations requiring vector control for Chagas disease and dengue and mass treatment for yaws need to be mapped out; current evidence indicates that these can be highly effective interventions in lower-middle-income and upper-middle-income endemic countries.

Our estimates suggest that the costs of ending NTDs are affordable globally (for example, US\$750 million per year in 2015–20 and US\$300 million per year in 2020–30, for preventive chemotherapy against five NTDs) and affordable for the governments of most endemic countries at less than 0.1 percent of domestic health spending. The estimated benefits to affected individuals in averted OOP health expenditures and lost productivity exceed US\$342 billion over the same period. The end of NTDs offers a net benefit to affected individuals of about US\$25 for every dollar invested by funders—a 30 percent annualized rate of return. It is a fair and efficient

investment in universal health coverage and social protection for the least well-off.

We compared NTDs with other public health programs by revisiting the Grand Convergence in Health by 2030, as proposed by the *Lancet* Commission on Investing in Health. Here the comparison is striking: ending NTDs would avert about 4 percent of the convergence total of 130 million deaths, and it would do so for less than 1 percent of the total convergence cost. This makes excellent health and economic sense on its own, but it is an underestimate of the true scale of benefit given that it ignores the 96 percent of health gains attributable to averted disability, rather than death, which is equivalent to about 519 million DALYs averted from 2015 to 2030.

Coordinated efforts to end the NTDs are emerging as among the largest public health programs in the world, and the most cost-effective and affordable. Indeed, the global program costs are on the scale of a rounding error at less than 1 percent of the grand convergence investment, yet offer a substantial return on investment. Furthermore, because these are diseases of poverty, the NTD agenda is specifically pro-poor; because the programs target morbidity, they are also specifically pro-development. All in all, this suggests that NTD programs have a special role in leading the world's efforts toward more fairness in health and the attainment of the SDGs.

NOTE

World Bank Income Classifications as of July 2014 are as follows, based on estimates of gross national income (GNI) per capita for 2013:

- Low-income countries (LICs) = US\$1,045 or less
- Middle-income countries (MICs) are subdivided:
 - (a) lower-middle-income = US\$1,046 to US\$4,125
 - (b) upper-middle-income (UMICs) = US\$4,126 to US\$12,745
- High-income countries (HICs) = US\$12,746 or more.

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